

## AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 2, line 4, as follows:

The MUC1 gene product is a high molecular weight (MW>200kDa) transmembrane glycoprotein expressed on the apical surface of many simple epithelial cells. It has a relatively large extracellular domain varying from 1000 to 2200 amino acids and a cytoplasmic tail of 69 amino acids. The extracellular domain consists mainly of tandem repeats of the 20 amino acid sequence PDTRPAPGSTAPPAHGV TSA, set forth as SEQ ID NO:1 [for a review, see Apostolopoulos & McKenzie (1994) *Crit. Rev. Immunol.*, 14: 293-309]. Variability in the number of repeats accounts for the variability in the size of the extracellular domain. Each repeat contains five potential O-linked glycosylation sites and two or possibly three of these sites are believed to be utilised.

Please replace the paragraph beginning on page 10, line 8, as follows:

The mucin peptide may be of the general formula "(aa)<sub>x</sub>PDTRP(aa)<sub>y</sub>" (SEQ ID NO:2) or "(aa)<sub>x</sub>APDTR(aa)<sub>y</sub>" (SEQ ID NO:3) where aa is an amino acid residue, the same or different in each position, x is an integer from 0 to 1000, and y is an integer from 0 to 1000. Preferably x is an integer from 0 to 500, more preferably 0 to 100, most preferably 0 to 10, and y is an integer from 0 to 500, more preferably 0 to 100, most preferably 0 to 10.

Please replace the paragraph beginning on page 10, line 13, as follows:

It is most preferred that the sequence "PDTRP" (SEQ ID NO:2) or "APDTR" (SEQ ID NO:3) is located towards the middle of the mucin peptide sequence of interest (as for example in the MUC1(16) defined hereinafter). Alternatively, the peptide sequence "PDTRP" (SEQ ID NO:2) or "APDTR" (SEQ ID NO:3) may be located towards the beginning of the mucin peptide sequence of interest (as for example in the MUC1(23) defined hereinafter). The above sequences/partial sequences are based on the 20 amino acid tandem repeat sequence of the extracellular domain of PEM.

Please replace the paragraph beginning on page 12, line 9, as follows:

~~Fig. 3~~ Fig. 3A shows the extent of staining of tumour cells by serum from mice immunized with CVPs in Freund's complete adjuvant (FCA), while Fig. 3B shows the extent of staining of tumour cells by serum from mice immunized with CVPs in QS-21. ~~of the invention.~~ Results are expressed as mean fluorescence intensity (MFI).

Please replace the paragraph beginning on page 12, line 22, as follows:

Fig. 8A shows the nucleotide (SEQ ID NO:8) and protein (SEQ ID NO:9) sequences of the SBMV coat protein (starting at nucleotide 3955) spanning a potential insertion site. The bold nucleotides show base changes used to introduce new restriction sites. Fig. 8B shows the nucleotide (SEQ ID NO:10) and protein (SEQ ID NO:6) sequences of MUC1(16), as well as a series of sequences to be inserted between the restriction sites of the SBMV coat protein. ~~to insert the MUC1(16) epitope at various locations.~~ In the five constructs shown, the MUC1(16) epitope sequence is inserted between SBMV coat protein amino acids 251-252 (SEQ ID NO:11), 252-253 (SEQ ID NO:12), 253-254 (SEQ ID NO:13), 254-255 (SEQ ID NO:14), and 255-256 (SEQ ID NO:15).

Please replace the paragraph beginning on page 12, line 26, as follows:

Fig. 9 shows a comparison of the  $\beta$ H- $\beta$ I loop of three sobemoviruses: LTSV (SEQ ID NO:16); SBMV (SEQ ID NO:17); and SMV (SEQ ID NO:18). Conserved residues are highlighted in bold and the locations of the loops (=) and  $\beta$ -strands (#) are indicated.

Please replace the paragraph beginning on page 12, line 28, as follows:

~~Fig. 10 shows the same as Fig. 8, but for~~ Fig. 10A shows the nucleotide (SEQ ID NO:19) and protein (SEQ ID NO:20) sequences of the LTSV coat protein (starting at nucleotide 3954) spanning a potential insertion site. The bold nucleotides show base changes to introduce new restriction sites. Fig. 10B shows the nucleotide (SEQ ID NO:10) and protein (SEQ ID NO:6) sequences of MUC1(16), as well as a series of sequences to be inserted between the restriction sites of the LTSV coat protein. In the six constructs shown, the MUC1(16) epitope sequence is inserted between LTSV coat protein amino acids 218-219

(SEQ ID NO:21), 219-220 (SEQ ID NO:22), 220-221 (SEQ ID NO:23), 221-222 (SEQ ID NO:24), 222-223 (SEQ ID NO:25), and 223-224 (SEQ ID NO:26).

Please replace the paragraph beginning on page 13, line 1, as follows:

Fig. 11 shows a Lipman-Pearson alignment of the coat protein sequences of RCNMV (SEQ ID NO:28) and TBSV (SEQ ID NO:27) ~~coat proteins~~.

Please replace the paragraph beginning on page 13, line 3, as follows:

Fig. 12 shows a Chou-Fasman  $\beta$ -region prediction plot for RCNMV coat protein residues 214-254 (SEQ ID NO:29), using an algorithm based upon the structures found in 64 proteins.

Please replace the paragraph beginning on page 13, line 5, as follows:

Fig. 13 shows the application of the EMBL PHDsec algorithm program to part of the ~~same~~ RCNMV (SEQ ID NO:30) sequence ~~shown in Fig. 12~~. "AA" shows the amino acid sequence; "PHD sec" indicates "profile network prediction Heidelberg" of secondary structure, with "H" indicating helix and "E" indicating extended (sheet); "Rel sec" indicates the reliability index of the prediction; "prH", "prE" and "prL" indicate the probability for assigning a helix, strand ~~of loop~~ or loop; "SUB" indicates a subset of the prediction, for all residues with an average expected accuracy of >82%.

Please replace the paragraph beginning on page 13, line 13, as follows:

~~Fig. 14 shows the same as Fig. 8, but for~~ Fig. 14A shows the nucleotide (SEQ ID NO:31) and protein (SEQ ID NO:32) sequences of the RCNMV coat protein (starting at nucleotide 3070) spanning a potential insertion site. The bold nucleotides show base changes to introduce new restriction sites. Fig. 14B shows the nucleotide (SEQ ID NO:10) and protein (SEQ ID NO:6) sequences of MUC1(16), as well as a series of sequences to be inserted between the restriction sites of the RCNMV coat protein. In the six constructs shown, the MUC1(16) epitope sequence is inserted between RCNMV coat protein amino acids 221-222 (SEQ ID NO:33), 222-223 (SEQ ID NO:34), 223-224 (SEQ ID NO:35), 224-225 (SEQ ID NO:36), 225-226 (SEQ ID NO:37), and 226-227 (SEQ ID NO:38).

Please insert the following paragraph beginning on page 32 (following the claims):

Mucin peptide epitopes are inserted into the coat protein of a plant virus (e.g., a comovirus such as CPMV) having a beta-barrel structure at an immunogenically effective site, such as in a loop connecting beta sheets or at/near the C-terminus. The resulting chimaeric virus particles are extremely immunogenic, giving better results than KLH conjugation and not requiring the addition of exogenous adjuvant. They are effective at mucosal surfaces, particularly when administered intranasally.